IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Maria Elena FERRERO — Conf. 3886

Application No. 10/589,621 — Group 1623

Filed October 6, 2006 — Examiner L. Crane

THE USE OF O-ATP FOR THE TREATMENT OF DISEASES INVOLVING ANGIOGENESIS

DECLARATION UNDER RULE 132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Maria Elena Ferrero, hereby declare as follows:

My relevant background and experience are set forth on the attached c.v.

I make this declaration in support of the present application, and to provide evidence in rebuttal of the contention set forth in the outstanding Official Action. The Official Action stated that the previously filed Declaration of June 18, 2008 did not disclose treatment of a particular disease condition in a host.

I supervised experiments to demonstrate the treatment of a particular disease condition in a host using oATP:

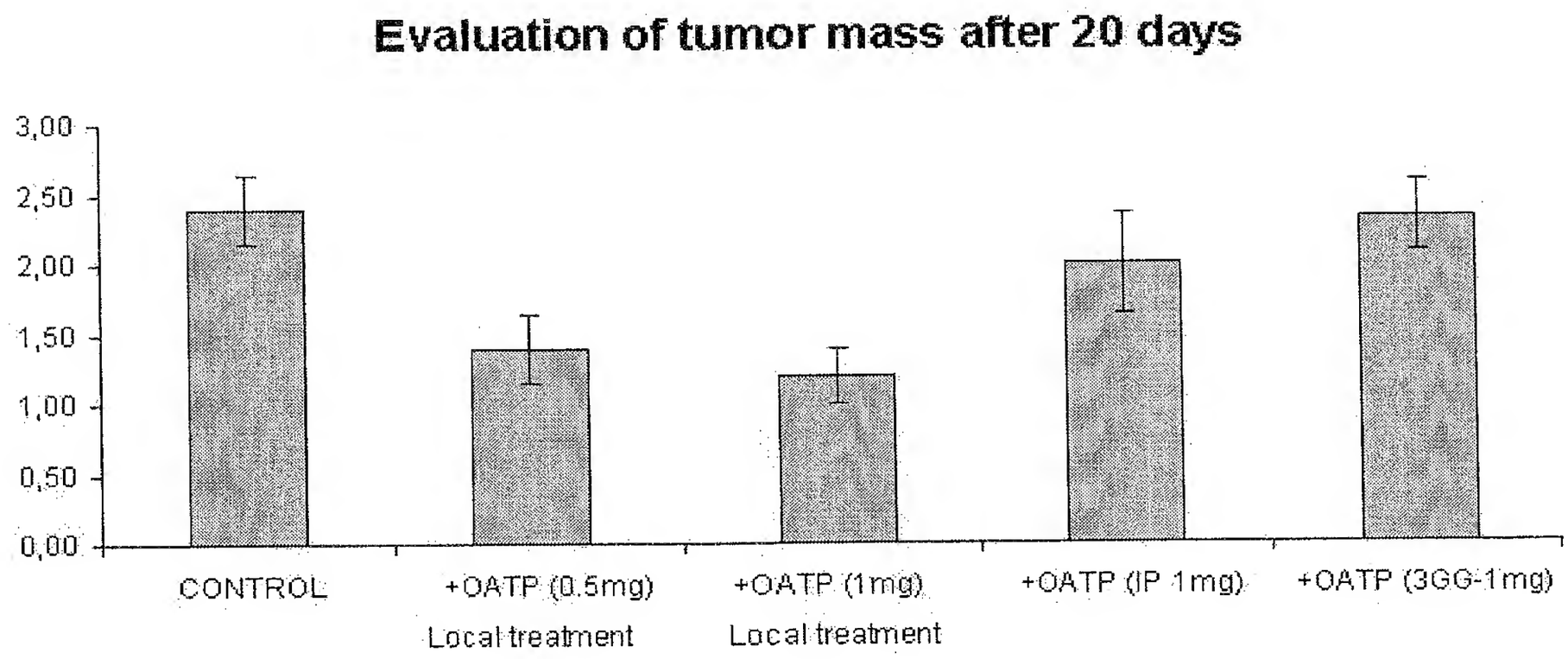
RMA cells were derived from the Rausher leukemia virus-induced mouse T-cell lymphoma RBL-5 of B6 origin and maintained in RPMI 1640 medium, supplemented with fetal bovine serum, 1% penicillin/streptomycin and 1% glutamine (complete medium).

C57BL/6 female mice weighing about 18-20 g (8 week old) were used. The cells were washed twice with 0.9% NaCl and subcutaneously injected in each mouse in a volume of 100 microliters containing 7x104 cells. After 10 days from RMA cell injection, we treated the mice with oATP. Five groups of mice were studied (each of 7 mice): 1) controls, untreated; 2) locally (subcutaneously) (sc) treated with 0.5 mg of oATP; 3) locally (sc) treated with 1 mg oATP; 4) intraperitoneally treated with 1 mg oATP; 5) locally (sc) treated with 1 mg oATP for 3 days only.

The mice were observed until the 20th day from the tumor inoculation: they were weighed daily and the size of the tumor mass was daily measured.

The tumor mass (measured by arbitrary units) did not significantly grow in the groups 3 and 5 for three days from the beginning of the treatment (e.g., until the 14th day) (data not shown). Successively, the control of the tumor growing is mainly exerted until the number of the tumor cells is not exponentially expanded. However, at 20 days from RMA cell injection, in the group 3 the tumor growth was less evident than that observed in the other groups (see the figure below). In addition, the tumor

mass obtained in 20 days in the mice from groups 3 was less solid than the tumor mass obtained in the other groups.



No significant differences were observed between the body weights of the mice measured during the different treatments (data not shown).

Our data shows that the local continuous treatment with 1 mg oATP is efficient in significantly slowing the tumor growth. It is possible that more elevated doses of oATP necessitate to control the tumor growth in the time.

Our in vitro data suggest that elevated concentrations of oATP (1 mg for about 70,000 RMA cells) are able to induce the apoptosis of these cells.

The undersigned declare further that all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Maria Elena Ferrero

Maria Elena FERRERO

May 4, 2009

Date

CURRICULUM VITAE - (MARIA ELENA FERRERO)

PERSONAL

Citizenship, Italian.

EDUCATION

High School Diploma (Maturità Classica),
1980-M.D. (110 laude/110 votes) Medicine and Surgery, University of Milan,
1984-Specialization (70 laude/70 votes) in Anesthesia and Ranimation.

EXPERIENCE

1985 Assistant Professor of General Pathology, Institute of General Pathology, University of Milan, Italy
1990 Associate Professor of General Pathology
2003 Full Professor of General Pathology and Pathophysiology

MEMBERSHIP

Member Biochemical Society of London
Member, European Society for Organ Transplantations
Member of Italian Society of Physiopathologists

PUBLICATIONS

Author of 138 publications
Author of 119 abstracts presented at International and National Congresses